79. The method of claim 64 wherein said one or more receptacles comprises a well plate.

80. The method of claim 66 wherein said one or more receptacles comprises is a well plate.

REMARKS

Applicants wish to thank the Examiner for the courtesy of an interview on March 31, 2003. At the Examiner's request, Applicants are submitting the Affidavit of Dr. G. Patrick Stahly with respect to certain points addressed during the interview.

Claims 1-33, 35, 38-41, 46-48 and 50-80 are pending in the present application after entry of the foregoing amendments. Claims 1-56 were all rejected in the Office Action of December 4, 2002. Claims 57-80 have been added by the present amendment.

Objection To The Title

The new title is similar to one of the titles proposed on page 2 of the Office Action. Applicants therefore believe the new title should be acceptable. Applicants submit that the amendment has no effect on the scope or nature of the invention.

Revisions to the Field of the Invention

At the Examiner's suggestion, Applicants have revised the Field of the Invention in an effort to improve the clarity of the application. The revision has no effect on the scope or interpretation of the claims.

Revisions to Example 1

On review of the specification, Applicants have discovered an inadvertent error in the description of Example 1. Applicants are amending Example 1 so that its details are accurate. Applicants submit that the amendment has no effect on the scope or nature of the invention.

Rejection of Claim 41 Under 35 U.S.C. §112, first paragraph

Claim 41 was rejected under 35 U.S.C. §112, first paragraph, based on the issue of the scope of enablement. (Office Action, pp. 3 and 9). In the interview of March 31, 2003, the Examiner indicated that the claim would be allowable if it was amended to delete the reference to biological activity. Applicants have made the suggested amendment to claim 41.

Rejection of Claims 1-56 Under 35 U.S.C. §112, second paragraph

Claims 1-56 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for various reasons. First, claim 1 was rejected because the language "a method of searching for possible forms of a sample" was allegedly unclear. In an earlier Office Action, it was asserted that "a method for screening possible forms" was more appropriate. Applicants have amended claim 1 to recite a method of screening for possible solid forms.

Applicants have also deleted claims 34, 37, 42-45 and 49 without prejudice or disclaimer in an effort to avoid having an unnecessary number of claims.

Next, claims 1 and 34 were rejected because they recite "forms" of a sample, which was said to be an indefinite term. Applicants submit that "forms" has a plain and ordinary meaning in the art that is recognizable to one of ordinary skill based on the present application. Nonetheless,

Applicants have amended claim 1 to clarify that solid forms are intended. This amendment does not alter the scope of the claims from their original scope.

Claims 26 and 27 were rejected as unclear, and the Examiner asked what it meant that the centrifuging is sufficient to facilitate in-situ analysis or to provide environmental variation. Applicants have amended these claims to include different language from the specification, which the Examiner may consider clearer.

Claim 53 was rejected as indefinite based on the language "wherein the analytical result is indicative of form." Applicants have amended claim 53 to clarify that is the solid form of the generated solids that is analyzed.

Claim 54 was rejected as indefinite, though the Examiner indicated that Applicants' remarks regarding that claim were clear. Applicants have amended claim 54 so that it is phrased in the language found in Applicants' remarks, which was deemed acceptable in the December 4, 2002 Office Action. This amendment is for clarification only and does not change the scope of the claim.

Applicants submit that the foregoing amendments and remarks overcome the rejections of the claims based on 35 U.S.C. §112, second paragraph. Applicants request that the rejections be withdrawn.

General Response To Prior Art Rejections

Claims 1-40, 42-53 and 55 were rejected on various prior art grounds. In the interview of March 31, 2003, Applicants explained that the cited references did not disclose the claimed methods, and the Examiner agreed that the references of record were inapplicable. Accordingly, Applicants respectfully request the Examiner withdraw the rejections directed to these claims.

New Claims 57-80

Applicants have added new claims 57-80 in the present Amendment. Claim 57 relates to generating a semisolid and is supported by the specification at, for example, page 9, lines 19-23; page 11, lines 23-26; page 14, lines 13-17 and 29-32; page 16, lines 1-3; page 17, lines 9-15; page 20, lines 27-29; in the Examples and the original claims.

New claims 58-66 and 77-80 relate to the use of a well plate that defines a plurality of capillary spaces. Claims 58-66 and 77-80 are supported by the specification at, for example, page 11, lines 8-11; page 13, lines 28-30; and Example 4.

Claims 67-70 relate to generating a melt, solidifying the melt, and analyzing the solid in a manner indicative of its form. Claims 67-70 are supported by the specification at, for example, page 16, lines 9-15 and 28-30.

New claims 71-72 relate to using transmission x-ray diffraction to analyze solid forms of the invention. Support for these claims may be found at, for example, page 26, lines 14-16.

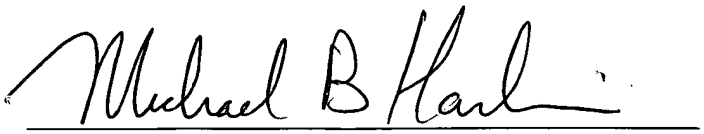
New claims 73-76 relate to receptacles made of polymer or glass. Support for these claims may be found at, for example, page 13, lines 30-32.

* * * * *

In view of the foregoing amendments and remarks, applicants submit that claims 1-33, 35, 38-41, 46-48 and 50-79 are allowable. The Examiner is invited to telephone the applicants' undersigned attorney at (312) 775-8202 or Eyal H. Barash at 202-408-4401 if any unresolved matters remain.

Please charge any additional fees incurred in connection with this submission to Deposit Account No. 13-0017.

Respectfully submitted,



Date: April 4, 2003

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EXHIBIT A
MARKED-UP VERSION SHOWING AMENDMENTS

IN THE TITLE:

Delete the original title and substitute in its place:

METHODS OF SCREENING FOR POSSIBLE SOLID FORMS

IN THE SPECIFICATION:

Under "FIELD OF THE INVENTION":

The present methods relate to **screening** **[searching]** for possible **solid** forms of a sample and include solidifying the sample in at least one receptacle defining a capillary space**, such as a capillary tube or well plate**. The present methods also relate to screening a sample according to its **solid** forms and include solidifying the sample in a plurality of receptacles, and at least one receptacle defines a capillary space. The **solid** form of the sample refers to its arrangement at the molecular or atomic level in the solid. **[The forms generated by solidification comprise solid forms and semisolid forms.]** The **[generated]** **solid** forms **generated by the solidification step** are analyzed and classified, such as by x-ray diffraction patterns. The present methods increase the likelihood of generating all or a high percentage of possible **solid** forms.

At page 22, lines 1-17:

The resulting capillaries containing solid or semisolid material were analyzed by laboratory x-ray powder diffraction in the capillary tubes without isolation of material using an INEL XRG 3000 diffractometer. Analysis of the x-ray diffraction data showed **[four]** **two** different x-ray powder patterns: the original crystalline form reported in the literature, **[two]** **and one** new crystalline powder patterns **[, and one amorphous pattern]**. These **[four]** **two** different x-ray diffraction patterns are indicative of **[four]** **two** different solid forms. A comparative study of 4-(6-methoxy-2-naphthyl)-butan-2-one using 80 traditional screening conditions (including crystallization in vials, varying solvents, varying conditions including fast evaporation, slow cooling, and crash cooling) showed only **[one new]** **the** diffraction pattern **of the original solid form reported in the literature**.

IN THE CLAIMS:

Claims 1, 7, 16, 26-27, 35, 38-41, 46-48, and 50-54:

1. A method of **[searching]** **screening** for possible **solid** forms of a sample, said method comprising the steps of:

disposing the sample on one or more receptacles, where at least one of the receptacles defines a capillary space, and the sample is disposed within the capillary space;

solidifying the sample in or on said receptacles to generate at least one **solid** form **[, wherein said at least one form is a solid or semisolid]**;

analyzing said at least one **solid** form in a manner wherein the analytical result is indicative of the generated **solid** form; and

classifying said at least one **solid** form.

7. The method of claim 1 wherein the **[compound] sample** is placed in at least 100 receptacles defining capillary spaces.

16. The method of claim 13, wherein the **spectroscopic analysis is [step of analyzing said form comprises]** Raman **spectroscopy [spectroscopic analysis]**.

26. The method of claim 24 wherein said centrifuging is sufficient to **concentrate the generated form [facilitate in-situ analysis]**.

27. The method of claim 24 wherein **two or more samples are centrifuged at different speeds or for different lengths of time [said centrifuging is sufficient to provide environmental variation]**.

35. The method of claim **[34] 1**, further comprising the step of determining whether more than one solid form was generated from said sample.

38. The method of claim **[34] 1** wherein the sample comprises a known polymorphic material.

39. The method of claim **[34] 1** wherein the sample comprises at least one material that is not recognized as being polymorphic.

40. The method of claim **[34] 1** wherein a plurality of samples are screened.

41. The method of claim **[34] 1** wherein a second analyzing step is performed on said generated form, said second analyzing step providing data indicative of **[biological activity or]** bioavailability.

46. The method of claim **[45]** **11**, wherein the analyzing step comprises analyzing said **at least one solid** form by X-ray diffraction analysis using synchrotron radiation as the radiation source for said analysis.

47. The method of claim **[45]** **11**, wherein the step of analyzing said **at least one solid** form comprises Raman spectroscopic analysis.

48. The method of claim **[45]** **11**, wherein the step of analyzing said **at least one solid** form comprises analyzing said form without removing it from said capillary tube.

50. The method of claim **[34]** **1**, wherein said classifying step comprises classifying **[each]** said **at least one** **[generated]** solid form according to its x-ray diffraction pattern.

51. The method of claim **[34]** **1**, further comprising subjecting a plurality of samples to the screening method, wherein at least two different samples are subjected to different conditions during the solidifying step.

52. The method of claim **[34]** **1**, comprising the step of dividing the sample into a plurality of sample portions, and subjecting said plurality of sample portions to the screening method, wherein at least two different portions are subjected to different conditions during the solidifying step.

53. A method of screening a sample, said screening method comprising the steps of:

disposing the sample on a plurality of capillary tubes;

centrifuging the plurality of capillary tubes;

solidifying the sample in the capillary tubes;

analyzing the solids in the capillary tubes in a manner wherein the **[a]** analytical result is indicative of **the solid** form **of the solids**; and

classifying each of the solids according to **the solid** form **of the solids**.

54. The method of claim 53, wherein **at least part of** said centrifuging step **occurs [is at least partially]** during said solidifying step.

EXHIBIT B
PENDING CLAIMS 1-33, 35, 36, 38-41, 46-48 AND 50-79

1. A method of screening for possible solid forms of a sample, said method comprising the steps of:

disposing the sample on one or more receptacles, where at least one of the receptacles defines a capillary space, and the sample is disposed within the capillary space;

solidifying the sample in or on said receptacles to generate at least one solid form;

analyzing said at least one solid form in a manner wherein the analytical result is indicative of the generated solid form; and

classifying said at least one solid form.

2. The method of claim 1 wherein the sample consists essentially of a solution of one compound.

3. The method of claim 1 wherein the sample comprises a mixture of compounds.

4. The method of claim 1 wherein the sample is disposed on a plurality of receptacles, including at least two different types of receptacles.

5. The method of claim 4 wherein said at least one receptacle includes a receptacle that do not define a capillary space.

6. The method of claim 1 wherein the sample is placed in at least five receptacles defining capillary spaces.

7. The method of claim 1 wherein the sample is placed in at least 100 receptacles defining capillary spaces.

8. The method of claim 1 wherein the solidifying step comprises crystallizing the sample.

9. The method of claim 1 wherein the solidifying step is selected from the group consisting of solvent evaporation, cooling, heating, anti-solvent addition, gel diffusion, and thin-layer deposition.

10. The method of claim 1, further comprising the step of forming a supersaturated solution of the sample.

11. The method of claim 1 wherein the placing step comprises placing the sample into at least one capillary tube.

12. The method of claim 1 wherein the disposing step comprises placing the sample into a receptacle selected from the group consisting of a well plate, a block with holes or pores and a sheet with holes or pores.

13. The method of claim 1, wherein the analyzing step comprises a method selected from the group consisting of visual analysis, microscopic analysis, thermal analysis, diffraction analysis, and spectroscopic analysis.

14. The method of claim 13, wherein the diffraction analysis is x-ray diffraction analysis.

15. The method of claim 13, wherein the analyzing step comprises analyzing said form by X-ray diffraction analysis using synchrotron radiation as the radiation source for said analysis.

16. The method of claim 13, wherein the spectroscopic analysis is Raman spectroscopy.

17. The method of claim 1, wherein the step of analyzing said form comprises analyzing said form without removing it from said receptacle.

18. The method of claim 11, wherein the step of analyzing said form comprises analyzing said form without removing it from said capillary tubes.

19. The method of claim 18 wherein the analyzing step comprises analyzing said form by X-ray diffraction analysis using synchrotron radiation as the radiation source for said analysis.

20. The method of claim 1, further comprising the step of comparing the generated form to a known form.

21. The method of claim 1 wherein said generating step produces at least one form of the sample that is different than a known form of the sample.

22. The method of claim 1 wherein said receptacle is subjected to substantially constant motion during said generating step.

23. The method of claim 1 wherein said receptacle is rotated along its longitudinal axis during said generating step.

24. The method of claim 1 wherein said receptacle is subject to centrifuging during said generating step.

25. The method of claim 24 wherein said centrifuging is sufficient to concentrate the solid or semisolid at one end of a capillary space.

26. The method of claim 24 wherein said centrifuging is sufficient to concentrate the generated form in one end of the capillary space.

27. The method of claim 24 wherein two or more samples are centrifuged at different speeds or for different lengths of time.

28. The method of claim 24 wherein said centrifuging is sufficient to move the sample to the bottom of said receptacle when one end of said receptacle is closed.

29. The method of claim 1 wherein said receptacle is subject to centrifugal evaporation during said generating step.

30. The method of claim 29 wherein said centrifugal evaporation is sufficient to concentrate the solid or semisolid at one end of a capillary space.

31. The method of claim 29 wherein said centrifugal evaporation is sufficient to facilitate in-situ analysis.

32. The method of claim 29 wherein said centrifugal evaporation is sufficient to provide environmental variation.

33. The method of claim 29 wherein said centrifugal evaporation is sufficient to move the sample to the bottom of said receptacle when one end of said receptacle is closed.

35. The method of claim 1, further comprising the step of determining whether more than one solid form was generated from said sample.

36. The method of claim 34, wherein said sample comprises a compound or mixture that has biological activity in at least one form of said compound or mixture.

38. The method of claim 1 wherein the sample comprises a known polymorphic material.

39. The method of claim 1 wherein the sample comprises at least one material that is not recognized as being polymorphic.

40. The method of claim 1 wherein a plurality of samples are screened.

41. The method of claim 1 wherein a second analyzing step is performed on said generated form, said second analyzing step providing data indicative of bioavailability.

46. The method of claim 11, wherein the analyzing step comprises analyzing said at least one solid form by X-ray diffraction analysis using synchrotron radiation as the radiation source for said analysis.

47. The method of claim 11, wherein the step of analyzing said at least one solid form comprises Raman spectroscopic analysis.

48. The method of claim 11, wherein the step of analyzing said at least one solid form comprises analyzing said form without removing it from said capillary tube.

50. The method of claim 1, wherein said classifying step comprises classifying each said generated solid form according to its x-ray diffraction pattern.

51. The method of claim 1, further comprising subjecting a plurality of samples to the screening method, wherein at least two different samples are subjected to different conditions during the solidifying step.

52. The method of claim 1, comprising the step of dividing the sample into a plurality of sample portions, and subjecting said plurality of sample portions to the screening method, wherein at least two different portions are subjected to different conditions during the solidifying step.

53. A method of screening a sample, said screening method comprising the steps of:

disposing the sample on a plurality of capillary tubes to generate solids;

centrifuging the plurality of capillary tubes;

solidifying the sample in the capillary tubes;

analyzing the solids in the capillary tubes in a manner wherein the a analytical result is indicative of the solid form of the solids; and

classifying each of the solids according to the solid form of the solids.

54. The method of claim 53, wherein at least part of said centrifuging step occurs during said solidifying step.

55. The method of claim 53, wherein said centrifuging step is performed at a pressure lower than ambient pressure.

56. The method of claim 53, wherein said centrifuging step is performed under vacuum.

57. A method of screening a sample according to its solid form, said screening method comprising the steps of:

disposing the sample on a plurality of receptacles, where at least one of the receptacles defines a capillary space, and the sample is disposed in the capillary space;

generating at least one semisolid from the sample in or on said receptacles;

analyzing the generated semisolid wherein the analytical result is indicative of the form of the semisolid; and

classifying the generated semisolid according to the indicated form.

58. A method of screening a sample, said screening method comprising the steps of:

disposing the sample on a well plate, wherein said well plate defines a plurality of capillary spaces, and the sample is disposed in the capillary spaces;

solidifying the samples in said capillary spaces to generate solids;

analyzing the generated solids to determine wherein the analytical result is indicative of the solid form of the generated solids; and

classifying the generated solids according to the indicated solid form.

59. The method of claim 58, wherein the step of analyzing the generated solids comprises analyzing without removing the generated solids from the receptacle in which the solids were generated.

60. The method of claim 59, wherein the analyzing step comprises x-ray diffraction analysis.

61. The method of claim 60, wherein the analyzing step comprises analyzing said generated solids by X-ray diffraction analysis using synchrotron radiation as the radiation source for said analysis.

62. The method of claim 58, wherein at least some of said capillary spaces are from about 0.1 mm to about 30 mm.

63. The method of claim 58 wherein at least some of said capillary spaces are from about 0.5 mm to about 17 mm.

64. The method of claim 58 wherein at least some of said capillary spaces are from about 0.5 mm to about 7 mm.

65. The method of claim 58, wherein at least some of said capillary spaces are from about 0.5 mm to about 5 mm.

66. The method of claim 58, wherein at least some of said capillary spaces are from about 0.5 mm to about 2.5 mm.

67. A method of generating and detecting possible solid forms, said method comprising the steps of:

generating a melt from a compound, element, or mixture;

disposing the melt on one or more receptacles defining a capillary space, and the melt is disposed in the capillary space;

solidifying the melt to generate at least one solid in or on said receptacles;

analyzing said at least one generated solid in a manner wherein the analytical result is indicative of the solid form of the generated solid.

68. The method of claim 64, wherein the compound, element or mixture is free of a solvent.

69. A method of generating and detecting possible solid forms, said method comprising the steps of:

melting a sample to form a melt;

disposing the melt on one or more receptacles defining a capillary space, wherein the melt is disposed in the capillary space;

forming a crystalline material from the melt in or on said receptacles;

analyzing said crystalline material in a manner wherein the analytical result is indicative of the solid form of the crystalline material.

70. The method of claim 64, wherein the melt is free of solvent.

71. The method of claim 60 wherein the analyzing step comprises transmission x-ray diffraction analysis.

72. The method of claim 14 wherein the analyzing step comprises transmission x-ray diffraction analysis.

73. The method of claim 1 wherein said at least one receptacle that defines said capillary space is made of polymer or glass.

74. The method of claim 57 wherein said at least one receptacle that defines said capillary space is made of polymer or glass.

75. The method of claim 64 wherein said one or more receptacles defining said capillary space is made of polymer or glass.

76. The method of claim 66 wherein said one or more receptacles defining said capillary space is made of polymer or glass.

77. The method of claim 1 wherein said one or more receptacles comprises a well plate.

78. The method of claim 57 wherein said plurality of receptacles comprises a well plate.

79. The method of claim 64 wherein said one or more receptacles comprises a well plate.

80. The method of claim 66 wherein said one or more receptacles comprises is a well plate.